Methods: The data base of the Krasnoyarsk branch of the National Hematology Research Center from Jan 2012 to Feb 2019 examination has been used. The *JAK2*V617F allele burden was measured in whole blood samples by an allele-specific quantitative polymerase chain reaction using of the "Myeloskrin JAK2 kit" (Formula of gene ltd). The relationship between the q (rate of JAK2 V617F detection) and the 1/T indicator ("reverse age") in each age-old five-year cohort on 1154 men and 958 women referred with suspicion of MPN was studied. The values of q^2 should be close to zero as according to the model of second order phase transitions for physical systems until reaching a certain critical patients age Tc and the relationship between the q^2 and 1/T variables will be described by the equation $q^2 = a\text{-}b/T$ with an angular coefficient b characterizing the increase in the intensity of the mutational burden with age after reaching the critical age T_c.
Results: Using of our model led to transforms the monotonous growth curve of mutation prevalence with age. The value of q^2 is close to zero at high values of 1/T (young patients) and for smaller values of 1/T (more older age) the relationship between q^2 and 1/T becomes linear (figure). The hypothesis of the statistical significance differences of regression for male and female was tested by Fisher test for the significance level a=5%. Hypothesis of the absence of differences between the two regressions is not rejected. The critical age of patients transition to the phase with a high risk of mutation development corresponds for male T_c = 48.8 years and for female T_c = 36.0 years. Intensity of further accumulation of the mutation burden in male b = 44.35 ± 12.86, in female b = 27.52 ± 4.57.
Summary/Conclusion: The "second order phase transitions model" it possible to introduce in the population analysis the indicators of the "critical age" T_c and the intensity of accumulation of the burden of mutations *b*. This estimate are not significantly different for male and female for our sample. The calculated critical age turned out to be significantly lower than the median of the age of diagnosis of MPN (53 and 57 years). The proposed model will be useful for analyzing the characteristics of the population of MPN in different cohorts, as well as in different social and environmental conditions of life.

PB2199 MESENCHYMAL STEM CELLS IN PH-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS: IDLE OBSERVERS OR PART OF THE DISEASE?

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Background: Pathogenesis in Philadelphia-negative Myeloproliferative Neoplasms (MPNs) is surely linked to genomic alterations in Hematopoietic Stem Cells (HSCs), most of all on genes which can carry mutations referred to as *driver mutations*: JAK2, CALR and MPL. Inflammation, neoangiogenesis and fibrosis are part of the clinical and biological picture of MPNs. Recent studies have hypotized a possible HSC-independent, active role of the Mesenchymal Stem Cells (MSCs) in the pathogenesis of these diseases.
Aims: Our aim is to characterize the molecular profile of bone marrow MSCs (BM-MSCs) of patients with diagnosis of MPNs to explore their possible contribution in the pathogenesis of the disease. In particular, we focused on the study of specific miRNA and mRNA already known in literature to be involved in processes of inflammation, neoangiogenesis and fibrosis in MPNs.
Methods: Primary cultures of BM-MSCs were obtained from bone marrow samples of patients with diagnosis of MPNs. Genic expression profile was evaluated with Real-Time Polymerase Chain Reaction compared to mesenchymal human healthy cell line.
Results: We found that some markers known to be involved in angiogenesis, as miR221, miR20a, HIF-1a and VEGF, are upregulated in BM-MSCs of MPNs patients. Regarding bone marrow fibrosis, expression analysis of THSB1, TGF-beta mRNAs and miR21 in BM-MSCs highlighted sensible upregulation in all samples, strongly suggesting a possible role of the MSCs in the mediation or induction of the fibrosis process in the bone marrow, in these diseases.
Summary/Conclusion: Our data suggest a possible role of the BM-MSCs in fibrosis and neoangiogenesis in MPNs. In subgroup analysis, clinical and histological presentations, it maybe that the study of the pathological MSCs will help comprehend the complex machine of pathogenesis in MPNs and possibly find new targets to develop drugs that may change the natural history of these diseases.

PB2200 PREVALENCE OF JAK2V617F, CALR AND MPL MUTATIONS IN PATIENTS OF MYELOPROLIFERATIVE NEOPLASMS AND SPLANCHNIC VEIN THROMBOSIS IN INDIA

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Background: Recurrent somatic mutations in the JAK2, MPL, and CALR genes have been described in patients diagnosed with Philadelphia-negative Myeloproliferative neoplasms (MPNs), including Polycythemia vera (PV), Essential thrombocythemia (ET) and Primary myelofibrosis (PMF). MPN is also the most common etiology in splanchnic vein thrombosis (SVT). MPNs account for approximately 40% of Budd Chiari syndrome (BCS) and 31% of portal vein thrombosis (PVT).
The present study was aimed at studying the prevalence of JAK-2V617F, MPLW515L/K and CALR exon 9 mutations in BCR-ABL1 negative myeloproliferative neoplasms (MPNs) and splanchnic vein thrombosis (SVT) patients.There is paucity of such data in the Indian patients.
Aims: The study had two **Aims:**
1. Identification of incidence of JAK2V617F, CALR exon 9 mutations and MPLW515L/K mutations in BCR-ABL1 negative MPNs in India
2. Identification of incidence of JAK2V617F, CALR exon 9 mutations and MPLW515L/K mutations in Indian patients of SVT
Methods: A total number of 60 patients of SVT and 59 MPN patients (10 PV, 19 ET, and 30 PMF) were included in the study. The mutation analysis for JAK2V617F, CALR exon 9 and MPLW515L/K mutations were performed using the Allele specific oligonucleotide-polymerase chain reaction (ASO-PCR) was used to detect JAK-2, CALR and MPL mutations.
Results: Among 59 patients of MPNs and 60 SVT; JAK-2 mutation was found in 61.0% (36/59) and 23.3% (14/60) respectively. On sub-classification, JAK-2 mutation was detected in 80.0% (8/10) of PV; 42.1% (8/19) of ET and 66.7% (20/30) of PMF patients.
All the patients of MPNs and SVT were subjected to CALR mutation analysis. The overall rate of CALR mutations in PMF and ET was 10% (3/30) and 21.0% (4/19) respectively. Limiting the analysis to JAK2V617F negative patients of PMF and ET, it was seen that 30% (3/10) PMF and ~36.36% (4/11) ET cases were CALR mutated. Of these 7 CALR mutations; L367fs*46 (type-1) and K385fs*47 (type-2) mutations were found in 5 and 2 patients respectively. MPL mutation was identified in 5.26% (1/19) ET cases. Triple negative ET and PMF were ~31.5% (~6/19) and ~23.3% (7/30) respectively. None of the SVT patients were observed to be CALR mutated and none showed the MPLW515L/K mutations.
Summary/Conclusion: Indian patients exhibit a lower incidence of CALR mutations in Primary myelofibrosis than that seen in the western literature. However, the incidence of CALR mutations is the same as that reported earlier in Indian patients of Essential thrombocythemia. Triple negative cases constitute 31.5% of all cases of Essential thrombocythemia and 23.3% of Primary myelofibrosis Indian patients show a Testing for CALR mutations and MPLW515L/K mutations in splanchnic vein thrombosis is not justified.

PB2201 PROGRESS AND SURVIVAL IN TRIPLE NEGATIVE PRIMARY MYELOFIBROSIS PATIENTS

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Background: Primary myelofibrosis (PMF) is a Philadelphia negative myeloproliferativ neoplasm characterized by a clonal myeloid expansion which determines progressive bone marrow fibrosis resulting in inefficient hematopoiesis. Diagnosis is based both on bone marrow morphology but also clinical aspects. There were described several mutations such as those in JAK_2 V617F, MPL exon 10 and CALR exon 9 indel genes in aproximately 90% of the patients while the rest of 10% were so-called triple negative.